PATENT COOPERATION TREATY



# PCT

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference<br>100886-1 WO | **FOR FURTHER ACTION** | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
|---|---|---|
| International application No.<br>PCT/SE 03/01703 | International filing date *(day/month/year)*<br>05.11.2003 | Priority date *(day/month/year)*<br>07.11.2002 |
| International Patent Classification (IPC) or both national classification and IPC<br>C07D295/155 | | |
| Applicant<br>ASTRAZENECA AB et al. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

| Date of submission of the demand | Date of completion of this report |
|---|---|
| 14.05.2004 | 15.12.2004 |
| Name and mailing address of the international preliminary examining authority:<br>European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465 | Authorized Officer<br>Usuelli, A<br>Telephone No. +49 89 2399-7366 |

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/SE 03/01703

## I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

**Description, Pages**

1-35 as published

**Claims, Numbers**

1-12 as published

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 9,10 (industrial applicability)

because:

☒ the said international application, or the said claims Nos. 9,10 relate to the following subject matter which does not require an international preliminary examination (specify):

**see separate sheet**

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Yes: | Claims | 1-12 |
| | No: | Claims | |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-12 |
| Industrial applicability (IA) | Yes: | Claims | 1-8,11,12 |
| | No: | Claims | |

2. Citations and explanations

**see separate sheet**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1- Claims 9-10 relate to subject matter considered by this Authority to be covered by the provisions of Rule 67.1 (iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of these claims, cf. Article 34(4)(a)(i) PCT.

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1- Reference is made to the following documents cited in the search report:

d1: WO 9723466
d2: WO 9315062

2- Novelty
Formulae (I) of d1 and d2 appear to overlap with present formula (I).
In particular,
- formula (I) of d1 overlaps with present formula (I) when:
G is N, R2-R6 are H, A is phenyl substituted with CONH2, B is a substituted aromatic, R1 is (C1-C6)-alkyl-B
- formula (I) of d2 overlaps with present formula (I) when:
G is N, R2-R5 and R7 are H, R6 is aralkyl, Ar is a 6-member carbocyclic aromatic ring substituted by Y, Y is CONR9R10, Z is carboxamide.
However, all the compounds disclosed in d1 and d2 lack at least two of the following features which are always present in the compounds of the invention: the group phenyl(CO)N(Et)2, the group phenyl(CO)NHR2 and the group CH2R1. Hence, present compounds can be regarded as novel since they derive from a multiple selection inside the prior art formulae.
None of the two documents disclose processes according to present claims 11 or 12.
Hence, the requirements of Art. 33.2 are met.

3- Inventive activity
3.1- The applicant has set himself the task of providing novel ligands of δ receptor which can be useful for the treatment of pain and gastrointestinal disorders.

The compounds of d1 are disclosed as ligands of δ receptor useful in the treatment of pain. Also the compounds of d2 bind the opiod receptors, in particular the δ and μ subreceptors.
D1 is taken as the closest prior art.
The data supplied on Table 1 of the application provide the evidence that present compounds selectively bound the δ receptor.
Hence, the objective technical problem can be regarded as the provision of further ligands of δ receptor.

3.2- The solution of this problem, represented by the compounds of formula (I) is regarded as obvious. As already stated above, present formula (I) is included, at least in part in formula (I) of d1. The skilled person, in the absence of any serious reason for doubting of the content of d1 would consider that substantially all the compounds encompassed by the formula (I) of this document possess the claimed activity, i.e. they are ligands of δ receptor. Hence, the mere fact of selecting a novel subclass of compounds inside the formula (I) of d1 and observing that the compounds of this subclass have the same activity disclosed in d1 for the whole formula (I) cannot be regarded as an activity involving an inventive skill.

The process of claims 11 and 12 are based upon common reactions, such as the alkylation of an amine and the hydrolysis of a nitrile, which are well known in the field of organic chemistry.
Hence, also these claims do not fulfil the requirements of Art. 33.3 PCT.